

DETAILED ACTION

The preliminary amendment, which included amendment to claims 1-7, filed on 07/13/2006, is made of record.

Information Disclosure Statement

References cited in the Information Disclosure Statement, filed on 07/13/2006, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Recitation of "extracted with an organic solvent incompletely miscible with water" in claim 1 renders claim 1 and its dependent claims 2-7 indefinite for more than one reason. First of all, when R¹ is hydrogen, the third choice of solvent R¹OH becomes HOH(water) and it cannot be said that water is incompletely miscible with water. The same is true for at least methanol and ethanol(R¹ is CH₃, CH₃CH₂). Similarly, when R¹ and R² are both hydrogen, the first choice R¹COOR² becomes HCOOH, formic acid, which is completely miscible with water. Same is true for acetic acid (R¹= CH₃ and R²= H). Furthermore, addition of calcium salt to acidic mixture when R² is hydrogen, would result in mixture of calcium salts derived from R¹-COOH and or neutralize the salt of

compound of formula I. Again, when R^1 and R^2 are methyl, the second choice is acetone which water miscible.

2. Recitation of "anti-solvent" in claim 1 renders claim 1 and its dependent claims 2-7 indefinite as it is vague and unclear as what is an anti-solvent.

3. Claim 3 is indefinite as the choice of R^1COOR^2 , when R^2 is hydrogen, includes acids while claim 3 requires an ester.

4. Claim 4 is indefinite as the choice of R^1COOR^2 , when R^2 is hydrogen, includes acids while claim 4 requires an ester.

5. Regarding claim 4, the phrase "preferably" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

6. Claim 5 and claim 6 are improper dependent claims on claim 1 as they fail to further limit claim 1. Note claim 1 does not recite R^1H and R^1OR^2 choices. Hence the scope of claim 5 and claim 6 is outside the scope of claim 1 on which it is dependent.

7. Recitation of "including" in claims 5-7, renders these claims indefinite as the term "including" is open and means more than what is being positively recited therein. See MPEP 2111.03 which states: The transitional term "including," which is synonymous with "comprising", "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named

elements are essential, but other elements may be added and still form a construct within the scope of the claim.); *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter*, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

8. Regarding claim 7, the phrase "particularly" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Instant process relates to process of making hemi-calcium salt of compound of formula I, wherein the key step is extraction of sodium or potassium salt of compound of formula I with an organic solvent and treating the organic extract with inorganic or organic calcium salt to obtain the said hemi-calcium salt. However, Examples 1-7 in the specification relate to sodium salt or potassium salt of rosuvastatin and there is no showing that the said calcium salt is made by the process. See example 1 which shows sodium salt of rosuvastatin and by analogy examples 3-7 show sodium salt of

rosuvastatin and example 2 again by analogy potassium salt. There is no showing that compounds of examples are hemi-calcium salts and example clearly shows it is not hemi-calcium salt.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Horbury et al., WO 2004/014872 (equivalent US2006/0116391) in view of Hirai et al., US 5,260,440 (equivalent EP 521,471) and Taylor et al., WO 00/49014.

Horbury teaches a process of preparing calcium salt of rosuvastatin, which process comprises mixing a solution of calcium chloride with a solution of water-soluble salt of rosuvastatin. See pages 1-8, especially lines page 2, lines 18-33. Note pages 2-8 provides further details of the process including the choice of water soluble salt and how

to obtain them and the various experimental parameters. See entire document for further details of the process. Particularly, see pages 19-24 for examples of the process.

Instant claims differ from Horbury et al., in requiring use of ester of rosuvastatin for making the water-soluble salt while Horbury is silent about hydrolysis of the ester to the water soluble salt. In addition, Instant claims require extraction of sodium salt and potassium salt into water-immiscible organic solvent before treating with inorganic or organic calcium salt.

Hirai teaches the hydrolysis of the methyl ester of rosuvastatin to obtain water soluble salt by treating it with sodium hydroxide and removing solvent under reduced pressure. See column 11, lines 30 through 68 and column 12 lines 1-10. See also instant specification, which acknowledges such a teaching. But specification does not show any comparative results to obviate any obviousness.

Taylor teaches a process for making calcium salt of rosuvastatin. See entire document. Especially see, page 2, third paragraph, wherein Taylor teaches the process of making calcium salt. Note use of solvent mixture and complete solution of calcium salt and its crystallization is taught therein. See example 7, which includes the process.

Thus, one having ordinary skill in the art at the time of the invention was made would have been motivated to combine both the primary and secondary references and employ the process taught by these prior art to esters of rosuvastatin, obtain the water soluble salt and use the water soluble salt to obtain the desired calcium salt including use of organic solvents for extraction and crystallization because he would have expected the analogous starting materials and reactants react similarly in view of the

combine teaching of the prior art. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note *In re Kerkhoven* 205 USPQ 1069.

Also see *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), wherein the court stated that [w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case with instant claims. Horbury teaches the process of making calcium salt of rosuvastatin, Hirai teaches the process of making the free acid and Taylor besides teaching the process of making calcium salt of rosuvastatin, teaches use of organic solvent for the process of crystallization. Hence, based on the combined teaching, which provide guidance to choose process parameters and reactants, one trained in the art would be motivated to employ the process taught by these prior art to esters of rosuvastatin, obtain the water soluble salt and use the water soluble salt to obtain the desired calcium salt including use of organic solvents for extraction and crystallization.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from

8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/
Primary Examiner, Art Unit 1624.